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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/571,405	03/10/2006	Christopher Norbert Johnson	PB60501	7796

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EXAMINER	
BERNHARDT, EMILY B	
ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
11/29/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/571,405	JOHNSON ET AL.	
	Examiner	Art Unit	
	Emily Bernhardt	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 8* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The abstract of the disclosure is objected to because it does not convey the structural makeup by way of a formula for applicants' invention. Correction is required. See MPEP § 608.01(b).

Claims 1,3 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. 1. The phrase for example, "e.g." appearing in the definition of optional substituents for R1 is not clearly defining the invention. Its not clear if the claims' scope are limited to up to 3 substituents or can have more as suggested by the term "one or more" preceding it.

Claims 1,3 and 8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for hydrates as solvates, does not reasonably provide enablement for remaining scope covered by "solvates". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The claims which all embrace any solvate are nonenabled since generally not all solvents can form solvates with all compounds. There is no process enabling such a scope in the specification nor is there any guidance as to what type of

solvents would be suitable for instant compounds other than mention of hydrates.

Claims 1,3 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following reasons apply.

1. Starting material sources for bridged piperazines resulting from the joining of two R2 groups at any location are not seen but are required. Specification is silent as to the availability of necessary reactants needed to prepare such ring systems of if they are commercially available. Note In re Howarth 210 USPQ 689; Ex parte Moersch 104 USPQ 122 for the need to show starting material sources commensurate with the claims' scope.

2. As there are no such fused compounds that have been made corresponding to the instant scope there is no reasonable basis for assuming that the myriad of compounds embraced by the all the generic claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no

basis in the prior art for assuming the same. The same applies for the scope of "A" rings which includes heteroaryls which can be monocyclic, bicyclic and /or mixed and directly or indirectly attached to the quinoline ring. Also the scope of substituents present at R1 and scope of rings covered by NR6R7 and NR8R9 include the same scope taught for "A" as well saturated analogs. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art.

Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition, which includes factors such as:

1) Breadth of the claims- the claims cover compounds easily in the millions as pointed out above;

2) Level of unpredictability in the art- the invention is pharmaceutical in nature as it involves binding to serotonin (5HT-6) receptors. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be unpredictable. See In re Fisher 166 USPQ 18;

3) Direction or guidance- the compounds made are not representative of the instant scope but are closer to each other than to remaining scope being always phenyl as "A" . At R1 scope which appears to be the advance over the art, only cycloalkyls and halobenzyl and a few haloalkyl groups have been made and tested;

4) State of the prior art- The compounds are piperazines located at the 8-position of quinoline which in turn are substituted at the 3-position with aromatic sulfonyls. While such compounds are known as evident from the closest art, WO'580, they are similar in structure to the compounds made herein and thus do not evidence the many structural permutations permitted in the instant scope are known for at least one use in the prior art;

5) Working examples- Actual test data has not been presented but it is stated that the examples have been tested and shown to have pKi values greater than 7 when tested for affinity towards human cloned 5-HT6 receptors and thus no clear evaluation of which functional groups at various positions out of the many claimed might affect potency to a large or small degree. Note Ahmed, a later commonly assigned article, describes

structure-sensitivity in a related series of compounds corresponding to the "A" variable. See p.4870,right column, 4th paragraph.

In view of the above considerations, this rejection is being applied.

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating anxiety,depression, schizophrenia and mild cognitive impairment, does not reasonably provide enablement for remaining uses covered by these claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The notion that simply having the ability to antagonize at 5HT6 receptor sites will enable the treatment of neurological disorders such as Alzheimer's or other age-related dementias, ADHD or obesity has not been substantiated by the current state of the art. While treating depression and schizophrenia has been reasonably linked to 5HT6 receptor binding since drugs that treat these uses have an affinity for this receptor, there is no basis in the pharmaceutical art for asserting all the uses being claimed. See Robichaud, provided by the examiner or Bromidge (ref.C3), provided by applicants, as examples of the current state of the serotonin receptor art. antagonists . There is no teaching that

treating Alzheimer's per se can be effected by such a class of antagonists. Note Rogers discusses the possibility of enhancing cognitive processes which in turn would provide **symptomatic** treatment for dementia. See p.114, right column. In searching Medline for obesity or ADHD and 5-HT6, no hits were found indicating evidence of one or more 5-HT6 antagonists undergoing clinical trials for these disorders. Thus the uses being urged are not all in currently available form based on the activity relied on and the specification provides only a starting point for further research. Note Genentech vs. Novo Nordisk 42 USPQ 2d 1001 especially left column at p.1005.

Note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition. Thus given the level of skill in this art which is low (for the treatment of all class of disorders being claimed) and the lack of direction (i.e. art-recognized tests) provided as to what might be treatable and in what dosage compounds are to be administered, this rejection is being applied.

Claim 2 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Commonly assigned WO'580 was found in a CAS structure search. It has been also cited by applicants. It lacks a teaching of the functional groups permitted at instant R1.

Applicants' IDS filed 3/10/06 cannot be fully considered at this time as none of the references are seen in the electronic file.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571-272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Emily Bernhardt/
Primary Examiner, Art Unit 1624